GENERAL MILLS
INSTITUTE
OF HEALTH
AND NUTRITION

November 18, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket Numbers 91N-100H, 91N-0101, 91N-0098, and 91N-0103; Food Labeling; Health Claims and Label Statements; Request for Scientific Data- Folic Acid (dietary supplement vs. food form) and Neural Tube Defects, Antioxidant Vitamins and Cancer, Fiber and Colorectal Cancer and Omega-3 Fatty Acids and Coronary Heart Disease.

Food and Drug Administration, HHS:

General Mills is a Delaware Corporation with its general offices at No. 1 General Mills Boulevard, Minneapolis, MN 55426. General Mills is a major packaged-food manufacturer engaged for over 60 years in the development and production of food products including flour, ready-eat-cereals, cake and other dessert mixes, snacks and numerous other products.

We have been committed to nutrition labeling for 25 years beginning with voluntary labeling of our consumer products in 1974. We currently have nutrition labeling on more than 600 products. Over the years, we have added additional information and claims to our products in response to consumer interest in newer knowledge about the relationship of diet and health. General Mills firmly supports changes in food-labeling practices that will provide consumers with nutrition information more relevant to today's needs.

Over the years, General Mills has supported the Agency's efforts to base health claims for foods and dietary supplements on sound scientific evidence. We believe that it is appropriate to re-evaluate the science concerning all four of the nutrient/disease relationships. Determining whether the data can delineate that these nutrients/components in a supplement have superior benefits compared to either foods fortified with these nutrients/components 'or foods that naturally contain them will be difficult. There have been significant advances in the scientific literature in each of these four health claims areas but we will focus our data submission related to folic acid and neural tube defects.

91N-0098

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Folic Acid and Neural Tube Defects

General Mills believes that the research published since 1992 regarding.folic acid and neural tube defects (NTD) has advanced the science significantly. Two areas where the research has grown is related to the bioavailability of synthetic versus naturally occurring folate and the level of folic acid that has an impact on NTD.

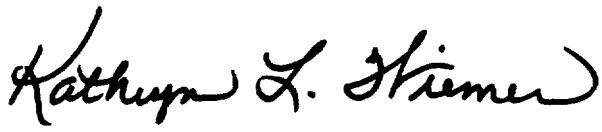
General Mills is submitting the enclosed references published since 1992 for the Agency's review and consideration. These published research papers pertain to clinical trials, bioavailability studies and summaries regarding folic acid from supplements and fortified foods and folic acid from naturally-occurring foods. Several of the studies indicate that the form of folic acid used in supplements and fortified food products have a comparable bioavailability, both of which are superior to naturally occurring folate in foods. Available research suggests that the bioavailability of naturally-occurring folic acid in food is approximately 50% of that from either supplements or fortified foods (IOM DRI Report, pre-pub, 1998). Estimated bioavailability of synthetic folic acid consumed with food is approximately 85 percent of that consumed without food based on experimental data.

An area where data is needed is **actual, current** dietary intake of the U. S. population since the initiation of mandatory enrichment of grain products with folic acid in January 1998. This data is critical to adequately determine what level of folic acid from a supplement is necessary for women of child-bearing age for the reduction of NTD. A 1999 study using two existing national databases estimated the intake of folic acid in the U. S. population (Lewis, et.al.). The study assessed the impact of the new folic acid values for fortified grain products, supplement intakes and the higher bioavailability of synthetic versus naturally occurring folate. Folic acid intakes for women of childbearing **age** improved **post-**fortification but fell below the recommended 0.4 mg. per day for synthetic folic acid. The study found, however, that many women of child-bearing age met or surpassed the Estimated Average Requirement (EAR) for folic acid recommended by the Institute of Medicine.

An up-to-date dietary assessment of folic acid intakes is essential before establishing a requirement of or a superiority claim for 0.8 mg. of folic acid from supplements versus common foods to reduce the risk of neural tube defects. Several recent studies suggest that folic acid intakes below 0.8 mg. have a significant, positive impact on neural tube defects and red cell folate. A recent study conducted in China indicates that 0.4 mg. synthetic folic acid (consumed in supplement form) significantly decreased the risk of neural tube defects in two regions, one with high and one with low rates of NTD. Dietary intakes were not measured but were considered a factor for existing differences in NTD rates between the two regions studied. In another study evaluating the impact of a fortified, ready-toeat cereal containing 0.1 mg., 0.4 mg. and 0.8 mg. of folic acid,

plasma folate levels were increased and blood homocysteine levels were decreased with statistical significance in the 0.4 and 0.8 mg folic acid cereal groups. We submit that additional data is needed to clarify whether 0.8 mg. is the appropriate level of folic acid to be specified in the health claim under consideration. Emerging research suggests that a lower level may be effective, especially given the impact of grain fortification. The upper tolerable level of 1 .O mg. should also be considered in this context. The claim may also be misleading in the context of today's eating patterns and food supply. Evidence is lacking to suggest that folic acid from a pill is superior to folic acid from fortified grain products.

Respectfully submitted,



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Enclosures